

Nitrate in Drinking Water Associated with Increased Risk for Non-Hodgkin's Lymphoma

Contamination of drinking water with nitrate, a chemical found in fertilizers, may be associated with an increased risk of non-Hodgkin's lymphoma (NHL), particularly in agricultural areas, a National Cancer Institute (NCI) study suggests.

In a study published in the September issue of the journal *Epidemiology*,* scientists from NCI, the University of Nebraska Medical Center in Omaha, and Johns Hopkins University in Baltimore assessed the average amount of nitrate consumed daily in tap water by Nebraska residents diagnosed with NHL, a cancer of the lymphatic system, and by a control group of persons without the disease who lived in the same area. Both groups used public water supplies.

The more nitrate they consumed in their water, the greater was their probability of developing NHL. Persons with NHL were twice as likely to be in the group that consumed the highest levels of nitrate as those without the cancer.

"This is one of the first epidemiologic studies to suggest a link between drinking-water nitrate and non-Hodgkin's lymphoma risk," said Mary H. Ward, Ph.D., of NCI, the study's lead author. "The findings deserve further evaluation because nitrate is a common contaminant of ground water in many areas of the country." However, it is uncertain whether the findings truly

*The study is titled "Drinking water nitrate and the risk of non-Hodgkin's lymphoma." Authors are M.H. Ward, S.D. Mark, K.P. Cantor, D.D. Weisenburger, A. Correa-Villaseñor, and S.H. Zahm. *Epidemiology*, September 1996.

reflect the effect of nitrate, she added. An alternate possibility is that nitrate exposure is simply a surrogate or “marker” variable that is correlated with some other NHL risk factor that was not directly measured in the study. (The researchers did assess occupational pesticide exposure, however, and determined that it could not account for their results.) NCI is conducting additional research that will help determine with greater certainty whether the association is real, and if so, how large it is.

Since 1973, incidence of NHL in the United States has increased about 75 percent—one of the largest increases among major cancer sites. An estimated 52,700 Americans will be diagnosed with the disease in 1996, and 23,300 will die from it. NCI has estimated that about 1 in 52 men and 1 in 61 women in the United States will be diagnosed with NHL during their lifetime, and that slightly fewer than 1 in 100 of both sexes will die of the disease.

Part of the increase in NHL incidence in recent years is a result of the AIDS epidemic: NHL is 60 times more common among AIDS patients than in the general U.S. population. Herbicides and insecticides have been linked to risk for NHL in studies of farmers, pesticide applicators, and other occupational groups exposed to high levels of these chemicals.

Nitrate forms N-nitroso compounds, many of which are known animal carcinogens. Biochemical studies in humans have shown that nitrate in water combines with amino acids to form these compounds.

The increase in mortality from NHL has been greatest in rural areas, a fact that could only be explained in part, by pesticide exposures in agricultural workers. The new findings on drinking-water nitrate among Nebraska residents who were not farmers suggest that nitrate, or some other exposure that is correlated with nitrate exposure, may be another NHL risk factor.

Earlier studies in Nebraska and China suggested that NHL and leukemia might be linked to nitrate intake, while a Danish study found no link between NHL and drinking-water nitrate.

Nitrate levels in ground and surface waters of agricultural regions have increased over the past 40 years as a result of increases in the use of nitrogen fertilizers. Nitrate contamination occurs in geographic patterns related to the amount of nitrogen contributed by fertilizers, manure, airborne sources, such as automobile and industrial emissions, and soil drainage characteristics. Areas with well-drained soils and high nitrogen inputs have the highest nitrate levels in the water supply. In particular, large areas of the Midwestern “corn belt” states have nitrate levels above natural levels. The U.S. Environmental Protection Agency’s (EPA) regulatory limit for nitrate is 10 mg per liter of drinking water.

One advantage of the new study—part of a larger case-control study that also examined associations between NHL and the herbicide 2,4-D, along with dietary and other possible risk factors—is that the researchers calculated nitrate consumption levels for each person rather than simply comparing cancer rates in large populations with differing nitrate levels in their water supplies. To do this, they determined from public records how much nitrate was in each person’s community water source starting in 1947, and asked subjects how much they typically drank each day of tap water, coffee, and other beverages made with tap water.

The researchers estimated drinking-water nitrate consumption for 90 women and 66 men diagnosed with NHL between 1983 and 1986 who used community water sources, and for a control group of 276 women and 251 men in the same eastern Nebraska counties who also used community water. Those with NHL were twice as likely to be in the group with the highest consumption levels of drinking-water nitrate (an average of 6.3 mg per day or more over their adult life) as those without the cancer. Persons exposed to drinking-water nitrate levels above

the EPA limit of 10 mg per liter for one year or longer—a group that made up 21 percent of all persons in the study—had a 50-percent higher risk than those having no exposure above this level.

A separate analysis of NHL cases and controls who used private well water found no association between NHL incidence and nitrate levels in well water. However, unlike community water sources, no long-term records of nitrate levels were available for private wells. Levels in wells were measured only once, at the time of the study, making it more difficult to determine cancer risk from nitrate exposure for persons using private water sources. Twenty percent of private wells exceeded the EPA recommended level. In general, persons using private wells are more likely to drink water containing high nitrate concentrations than persons using public water supplies, because of the simpler construction and shallower depth of private wells.

Nitrate intake from dietary sources was also estimated for each person in the study. Higher dietary nitrate consumption—mostly from vegetables including spinach, lettuce, and beets—was associated with lower risk for NHL. This apparently contradictory finding may be explained by the anticarcinogenic effects of vegetable components such as vitamin C and carotenes (vitamin A-related compounds).

NCI is further investigating the link between drinking-water nitrate and NHL in a series of case-control studies among residents of Iowa and Minnesota, other agricultural states that have areas of elevated groundwater nitrate levels. Nitrate consumption is also being studied as a possible risk factor for stomach cancer, a disease that is less common in the United States than in Asia and some other parts of the world.

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Sources of National Cancer Institute Information

Cancer Information Service

Toll-free: 1-800-4-CANCER (1-800-422-6237)

TTY (for deaf and hard of hearing callers): 1-800-332-8615

NCI Online

Internet

Use <http://www.cancer.gov> to reach NCI's Web site.

CancerMail Service

To obtain a contents list, send e-mail to cancermail@icicc.nci.nih.gov with the word "help" in the body of the message.

CancerFax® fax on demand service

Dial 301-402-5874 and listen to recorded instructions.

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